

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
19 May 2005 (19.05.2005)

PCT

(10) International Publication Number
WO 2005/044984 A3

(S1) International Patent Classification⁷: **A61K 38/00**

(21) International Application Number:
PCT/US2004/033874

(22) International Filing Date: 14 October 2004 (14.10.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/511,609 15 October 2003 (15.10.2003) US

(71) Applicant (for all designated States except US):
TRUSTEES OF DARTMOUTH COLLEGE [US/US]; Technology Transfer Office, 11 Rope Ferry Road, Hanover, NH 03755-1404 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **STANTON, Bruce, A. [US/US]; 26 Low Road, Hanover, NH 03755 (US). O'TOOLE, George, A. [US/US]; 5 Fletcher Circle, Hanover, NH 03755 (US). SWIATECKA-URBAN, Agnieszka [PL/US]; 1 South Park Street, #B, Hanover, NH 03755 (US). MACEACHRAN, Dan [US/US]; RR 1, bOX 151, Oxford, NH 03755 (US). MARQUIS, Sophie, Moreau [FR/US]; 51 Pemberton Road, Nachua, NH 03063 (US).**

(74) Agents: **LICATA, Jane, Massey et al.; Licata & Tyrrell P.C., 66 E. Main Street, Marlton, New Jersey 08053 (US).**

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
18 August 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2005/044984 A3

(54) Title: MODULATORS OF THE ABC TRANSPORTER FAMILY AND METHODS FOR THEIR USE

(57) Abstract: An isolated factor derived from the bacterium *Pseudomonas aeruginosa* that reduces expression of ABC transmembrane proteins and active fragments and mimetics thereof are provided. Also provided is a method for inhibiting expression of ABC transmembrane proteins in cells by administering to the cells the isolated factor or active fragment or a mimetic thereof. Such methods are useful in the enhancing delivery of small molecule therapeutic agents to the CNS and in treating cancers, particularly multidrug resistant cancers, and secretory diarrhea. In addition, compositions, methods for identifying compositions and methods for use of compositions which inhibit suppression of ABC transmembrane protein expression by this factor are provided. Such compositions and methods are useful in treatment of cystic fibrosis.